MINUTES OF THE LTLC MEETING OF 1-23-96

Attendees:	William Burnam	Karl Baetcke	Jess Rowland
	Jim Rowe	Mike Ioannou	Clark Swentzel
	Paula Deschamp	Debbie McCall	Jane Smith
	John Redden	Paul Chin	Yung Yang
	Bill Sette	Susan Makris	Tom Campbell
	Roger Gardner		

Chemicals Reviewed: Dibrodicyanobutane Phorate Aldicarb

FINAL DOCUMENT DUE DATE: 2/06/96

DIBROMODICYANOBUTANE

Broad spectrum microbicide - non food use

Dermal absorption: No studies available. Based on the results of the dermal studies, dermal absorption of any consequence is not expected. In the 21-day dermal toxicity study, the NOEL for dermal toxicity less than 1000 mg/kg/day.

Acute Dietary: Non food use; risk assessment not required.

Short-term: No appropriate endpoint of concern was identified. The test material is not absorbed via the dermal route as demonstrated by a 21-day dermal toxicity study in which no systemic toxicity was observed following repeated dermal application of the test material at 0, 1000, 2000 or 4000 mg/kg/day. For systemic toxicity, the NOEL was > 4000 mg/kg/day (HDT).

The lack of systemic toxicity is corroborated by the developmental toxicity studies in rats and rabbits which indicated that the test material is not a developmental toxicant. The NOEL for developmental toxicity was >175 mg/kg/day in rats (MRID # 249004) and 60 mg/kg/day in rabbits (MRID #4340502).

Intermediate: Not required. - use same rationale as above.

Chronic: Not required. use same rationale as above.

PHORATE

Food use chemical

Dermal absorption: No studies available. Dermal absorption should be 100% based on the acute oral LD50 of 2.71 mg/kg/day and dermal LD50 of 3 mg/kg/day in rats (ACCN # 114194).

Acute Dietary: Dose & endpoint selected: NOEL of 0.05 mg/kg/day; decreases in RBC and brain ChE activity and tremors were seen in both sexes of dogs at 0.25 mg/kg/day in a 1-year feeding study in dogs (MRID #4017452).

This dose was selected for acute dietary risk assessment because this dose/endpoint was used to establish the RfD and the ChE NOEL of this study (mentioned above) was comparable ChE NOELs observed in 90-day studies with rats and dogs (discussed below) in which ChE activity was measured after 6-days (rats) or 1 week (dogs). The 90-day studies were not used either in the assessment of RfD or the LTL because the confidence in these studies were low (old studies which did not follow the protocol/current guidelines) and were Core classified as Supplementary.

In a 90-day dietary feeding study with rats (MRID # 92873), plasma, RBC and brain cholinesterase inhibition (ChEI) measurements were made on Day 6. At 0.3 mg/kg/day males exhibited decreases in plasma, RBC and brain ChE while females at this dose had decreases in plasma and RBC ChE. The NOEL for ChEI was 0.1 mg/kg/day for both sexes. This 1955 study was classified as supplementary since the protocol did not adhere to the current guidelines.

In a 105-day dietary feeding study with dogs (MRID #92873), ChEI was determined at Week 1. Plasma ChE was decreased by approximately 50% at 0.05 mg/kg/day. The NOEL for ChEI was 0.01 mg/kg/day. This 1955 study was classified as supplementary due to non adherence to current guidelines.

Short-term: 0.05 mg/kg/day and 100% dermal absorption for risk assessment.

Intermediate: 0.05 mg/kg/day NOEL and 100% dermal absorption for risk assessment.

Chronic: 0.05 mg/kg/day NOEL and 100% dermal absorption for risk assessment.

Inhalation exposure: No appropriate acute or subchronic inhalation toxicity studies were available on the non-granular technical material. Consequently, phorate should be classified in Toxicity Category I and risk assessments for inhalation exposure should be inclusive of the inhalation (100%) and dermal (100%) exposures. The NOEL of 0.05 mg/kg/day used in the dermal risk assessments should also be used for this exposure scenario.

ALDICARB

Dermal absorption: No studies available. Although the oral LD50 of 1.3 mg/kg and the dermal LD50 of 5 mg/kg in rabbits indicate minimal dermal absorption, due to the low confidence in the data (i.e, purity of the test material was not known, values were for rabbits not rats, the vehicle used in both studies was propylene glycol, and data reviews were not available), a conservative estimate of 100% dermal absorption should be used for risk assessments.

Acute Dietary: Dose and endpoint: 0.001 mg/kg/day based on the NOEL of 0.01 mg/kg/day from an acute human exposure study and an uncertainty factor of 10. The LOEL of 0.025 mg/kg/day was based on sweating. This dose/study was also used to establish the RfD.

Additionally, the NOEL observed in humans in the above study is supported by the comparable NOELs observed in a 90-day study in dogs (NOEL= 0.009 mg/kg/day) and sunchronic neurotoxicity study in rats (NOEL = <0.05 mg/kg/day).

Short-term: dose/endpoint/rationale same as acute dietary

Intermediate-term: dose/endpoint/rationale same as acute dietary

Chronic: dose/endpoint/rationale same as acute dietary

Inhalation exposure: Due to lack of appropriate inhalation studies Aldicarb should be placed in Toxicity Category I. Risk assessments for inhalation exposure should be inclusive of the inhalation (100%) and dermal (100%) exposures. The dose for risk assessment should be 0.001 mg/kg/day (i.e., NOEL of 0.1 mg/kg/day from the human study and an UF of 10)